REMARKS

Claims 1-13 are pending in the application. The claims have not been amended by the present response.

Allowable Subject Matter

At page 5 of the Office Action, the Examiner stated that claims 3-5 and 11-13 are allowed. In view of the remarks presented herein, applicants respectfully submit that all of the pending claims are in condition for allowance.

35 U.S.C. §112, First Paragraph (Written Description)

At pages 4-5 of the Office Action, claims 1, 2, and 6-10 were finally rejected as containing subject matter that was not described in the specification in such a way that one skilled in the art can reasonably conclude that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action maintains this rejection, at least in part, based upon the assertion that

> Applicants' arguments and specification do not note which amino acids are critical to the disclosed function; which amino acids can be changed without destroying the conformation of the polypeptides and thus not allowing trigger dimerization of the receptor protein Ret and autophosphorylation of a tyrosine kinase domain of the receptor Ret; and what are the domains within SEQ ID NO: 17 and SEQ ID NO: 21 that must be maintained to facilitate the claimed functions.

Applicants respectfully traverse the rejection in view of the following remarks.

The present written description rejection was discussed in the telephone interview with Examiner Harris and the undersigned on December 12, 2007, as well as in several recent follow up telephone conversations. Examiner Harris emphasized in the interview that a response to this rejection should identify those portions of the RetL3 polypeptide that are expected to be amenable to change without eliminating the RetL3 bioactivity recited in the claims. Applicants respectfully submit that the following remarks and the RetL3 sequence alignment provided below establish that pending claims 1, 2, and 6-10 satisfy the written description requirement.

The present application describes the identification and characterization of two species of RetL3 proteins: the human RetL3 protein (SEQ ID NO:21); and the mouse RetL3 protein (SEQ ID NO:17). These two species of RetL3 are 76.8% identical to each other (see specification at page 37, paragraph 0116). An alignment of the amino acid sequences of the two RetL3 proteins is depicted below (* indicates those amino acid residues that are identical between the human and mouse RetL3 proteins).

```
human          MVRPLNPRPLPPVVLMLLLLLPPSPLPLAAGDPLPTESRLMNSCLQARRKCQADPTCSAA 60
mouse          MGLSWSPR---PPLLMILLLVLSLWLPLGAGNSLATENRFVNSCTQARKKCEANPACKAA 57
               *  . .**   * :**:***: .  ***.**:.*.**.*::*** ***:**:*:*:*.**

human          YHHLDSCTSSISTPLPSEEPSVPADCLEAAQQLRNSSLIGCMCHRRMKNQVACLDIYWTV 120
mouse          YQHLGSCTSSLSRPLPLEESAMSADCLEAAEQLRNSSLIDCRCHRRMKHQATCLDIYWTV 117
               *:**.*****:* *** **.::.********:********.* ******:*.:********

human          HRARSLGNYELDVSPYEDTVTSKPWKMNLSKLNMLKPDSDLCLKFAMLCTLNDKCDRLRK 180
mouse          HPARSLGDYELDVSPYEDTVTSKPWKMNLSKLNMLKPDSDLCLKFAMLCTLHDKCDRLRK 177
               * *****:**************************************************:********

human          AYGEACSGPHCQRHVCLRQLLTFFEKAAEPHAQGLLLCPCAPNDRGCGERRRNTIAPNCA 240
mouse          AYGEACSGIRCQRHLCLAQLRSFFEKAAESHAQGLLLCPCAPEDAGCGERRRNTIAPSCA 237
               ******** :****:** ** :********.***********:* ************.**

human          LPPVAPNCLELRRLCFSDPLCRSRLVDFQTHCHPMDILGTCATEQSRCLRAYLGLIGTAM 300
mouse          LPSVTPNCLDLRSFCRADPLCRSRLMDFQTHCHPMDILGTCATEQSRCLRAYLGLIGTAM 297
               **.*:****:** :* :********:**********************************

human          TPNFVSNVNTSVALSCTCRGSGNLQEECEMLEGFFSHNPCLTEAIAAKMRFHSQLFSQDW 360
mouse          TPNFISKVNTTVALSCTCRGSGNLQDECEQLERSFSQNPCLVEAIAAKMRFHRQLFSQDW 357
               ****:*:***:**************:*** **  **:****.********** *******

human          PHPTFAVMAHQNENPAVRPQPWVPSLFSCTLPLILLLSLW 400
mouse          ADSTFSVVQQQNSNPALRLQPRLPILSFSILPLILLQTLW 397
               ...**:*: :**.***:* ** :* *  . ****** :**
```

The alignment above (which is obtained by simply comparing the sequences of SEQ ID NO:17 and SEQ ID NO:21, both of which are disclosed in the specification) identifies both (i) those amino acid residues that are identical between the human and mouse wild-type RetL3 proteins, and (ii) those amino acid residues that differ between the two species. The skilled artisan would readily expect that, at a minimum, those particular amino acids that differ between the two wild-type RetL3 proteins (i.e., 23.2% of the amino acid positions) are likely to be amenable to change without eliminating biological activity. Similarly, those amino acids that do not differ between the two species are more likely to be associated with domains or motifs that

are required for the maintenance of RetL3 function. It is the provision in the specification of the amino acid sequences of these two divergent species of wild-type RetL3 proteins that allows a person of ordinary skill in the art to readily identify specific amino acids that can likely be changed without destroying the ability of a variant RetL3 polypeptide to interact with the receptor tyrosine kinase Ret.

Independent claim 1 is directed to an isolated polypeptide that (i) comprises an amino acid sequence that is at least 80% identical to the sequence of SEQ ID NO:17 or SEQ ID NO:21, and (ii) interacts with and triggers dimerization or autophosphorylation of the receptor protein Ret. As compared to the specification's disclosure of two species of RetL3 proteins that are 76.8% identical to each other, pending claims 1, 2, and 6-10 encompass variation (at a maximum of 20% of the amino acid positions) that is in fact less than that existing between the two disclosed RetL3 proteins (which vary at 23.2% of their amino acid positions).

The genus of polypeptides encompassed by claim 1 does not have substantial variation, since all such polypeptides must have a specified activity and contain a sequence that is at least 80% identical to SEQ ID NO:17 or SEQ ID NO:21. As noted above, the human and mouse RetL3 proteins disclosed in the specification are representative of the claimed genus because: all polypeptides encompassed by the claimed genus are required to be even more closely related (i.e., at least 80%, 90%, or 95% identical) to SEQ ID NO:17 or SEQ ID NO:21 than the variation (76.8% identity) that exists between the two RetL3 species exemplified in the application; and routine assays are well known in the art for identifying variants having the functional activity specified by the claim.

In light of the disclosure contained in the application as filed, the skilled artisan would have concluded that the inventors were in possession (at the time of filing of the present application) of the necessary common attributes possessed by the members of the claimed genus. Accordingly, applicants respectfully submit that independent claim 1 and claims 2 and 6-10 that depend therefrom satisfy the written description requirement. Applicants request that the Examiner withdraw the rejection.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is requested.

Enclosed is a Petition for Three Month Extension of Time. The extension of time fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 13751-045003.

Respectfully submitted,

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